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CASE CV0276a

CERTIFICATE OF MAILING

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being deposited with the United States Postal Service on the date shown below with sufficient postage as first class mail in an envelope addressed to the: Mail Stop Appeal Brief-Patents, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

John M. Kilcoyne	John M. Kilcoyne	May 3, 2005
Type or print name	Signature	Date

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE APPLICATION OF
Stewart A. Cederholm-Williams

Art Unit: 1632
Examiner: S.L. Chen

APPLICATION NO: 09/334,325
FILED: June 16, 1999
FOR: Fibrin Sealant as a Transfection/Transformation Vehicle for Gene Therapy

Mail Stop Appeal Brief-Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

TRANSMITTAL LETTER

Sir:

Enclosed herewith is an Appeal Brief in the above-identified application.

☒ The appeal fee has already been paid. The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment, to Account No. 02-3869 in the name of Bristol-Myers Squibb Company.

Respectfully submitted,

John M. Kilcoyne
Attorney for Applicant
Reg. No. 33,100

Bristol-Myers Squibb Company
Patent Department
100 Headquarters Park Drive
Skillman, NJ 08558
(908) 904-2372
Date: May 3, 2005

CASE CV0276a

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FOR: FIBRIN SEALANT AS A TRANSFECTION/TRANSFORMATION VEHICLE

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Alexandria, VA 22313-1450

APPEAL BRIEF

Sir:

This is an appeal from the Final Rejection of claims 1 and 13-16.

(1) REAL PARTY IN INTEREST

The real party in interest in this appeal is Bristol-Myers Squibb Company, a Delaware corporation, having a place of business at 345 Park Avenue, New York, NY 10154. Bristol-Myers Squibb Company is the assignee and owner of the entire interest in the above-identified application by virtue of an assignment which was recorded in the United States Patent and Trademark Office on August 23, 1999, at Reel/Frame 010191/0657.

(2) RELATED APPEALS AND INTERFERENCES

The undersigned knows of no other appeals or interferences which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) STATUS OF CLAIMS

Claims 1 and 13-16 are pending in this application.

Claims 1 and 13-16 stand rejected under 35 USC §112, first paragraph, as allegedly lacking enablement.

No claims are allowed.

Appendix A annexed hereto contains a copy of the claims involved in the appeal. The appealed claims are claims 1 and 13-16.

(4) STATUS OF AMENDMENTS

Appellant appeals the decision dated December 3, 2004, of the Primary Examiner finally rejecting claims 1 and 13-16. No amendments were filed after the final rejection. Accordingly, claims 1 and 13-16 remain pending in this application.

(5) SUMMARY OF CLAIMED SUBJECT MATTER

The present invention relates to a method of transforming a cell comprising, in order, the steps of applying a transformation effective amount of a nucleic acid to the cell; adhering a pliable, adhesive fibrin gel to the cell so as to entrap a transformation effective amount of the nucleic acid in the fibrin gel adhered to the cell; and transforming the cell with the nucleic acid. See, for example, page 2, lines 9-17, of the specification.

(6) GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

The sole issue on appeal is whether claims 1 and 13-16 were properly rejected under 35 USC §112, first paragraph.

(7) ARGUMENTS

I. Claims 1 and 13-16 were not properly rejected under 35 USC §112, first paragraph

Claims 1 and 13-16 stand rejected under 35 USC §112, 1st paragraph, as allegedly lacking enablement.

The rejection essentially asserts that "[t]he claims read on gene therapy *in vivo*", and since gene therapy was unpredictable at the time of the invention, the claims lack enablement. However, the claims are not directed to gene therapy *per se*. Rather, the claims are directed to transforming a cell. There is nothing in the rejection to say that *transforming a cell* is unpredictable. In fact, the rejection admits that "progress has been made" in many respects. Accordingly, it is submitted that this rejection is not directed to the claims as written and should therefore be withdrawn.

Moreover, although the issue presented in the rejection is whether appellant has enabled the invention, the basis of the rejection is an assertion that the application fails to demonstrate that the invention works. Thus, the 35 U.S.C. § 112 rejection is simply a rejection under 35 U.S.C. § 101 in the guise of a rejection under 35 U.S.C. § 112.

The Office asserts that the rejection is for lack of enablement under U.S.C. § 112, first paragraph, and is distinct from a rejection under U.S.C. § 101 asserting inoperability. Specifically, the Office asserts that

> the specification, while being enabling for a method of transforming a cell *in vitro* by applying a nucleic acid to the cell and then adhering a pliable, adhesive fibrin gel to said cell so as to entrap the nucleic acid in the fibrin gel to the cell, does not reasonably provide enablement for a method of transforming a cell *in vivo* by applying a nucleic acid to the cell and then adhering a pliable, adhesive fibrin gel to said cell so as to entrap the nucleic acid in the fibrin gel to the cell and transform said cell. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

It was asserted in a previous rejection that "[T]he specification fails to provide adequate guidance **and evidence** for transforming a cell *in vivo* by applying a nucleic acid, such as a vector or a virus carrying the nucleic acid, to the cell first and then applying a pliable, adhesive fibrin gel to said cell so as to transform the cell *in vivo* at any location of any subject. No teachings are present within the specification in regard to how to transform cells in a subject with any nucleic acid in any vector to any virus containing said nucleic acid by the claimed method steps."

It is still asserted in the final rejection that "[t]he specification fails to provide adequate guidance and evidence for how to administer a pliable, adhesive fibrin gel to a cell having administered nucleic acid in a subject **such that target cells in said subject are transformed with said nucleic acid**."

That the nature of the rejection focuses on the text presented above in added **bold** is clear from the text presented above in added underline. That is, the text in added underline acknowledges that the description of how to make the transforming composition is indeed in the application, that transforming nucleic acids are well-known, and that transforming a cell *in vitro* is enabled. Further, in previous rejections, it was acknowledged that transforming a cell *in vivo* is enabled when done with certain equipment. Implicit in these acknowledgements is that those of ordinary skill who have undertaken many transformations know how to measure for such transformation, and even have been enabled if they use a stent or balloon catheter. Yet, what is emphasized in **bold** is the Office's assertion regarding the specification's teachings relative to how the nucleic acid entrapped in fibrin gel can be taken up by cells.

Because the subject rejection is for want of utility, it is incumbent on the Office to present sufficient reason to doubt applicant's assertion of utility. One way to seek to conform to the legal requirements for such a rejection would be to follow the Office's own internal guidelines--the Utility Examination Guidelines. While the burden on the Office to justify an assertion of want of a credible utility would appear more relaxed in the guidelines than in the precedent of the Court of Appeals for the Federal Circuit, even this low hurdle was not met in the subject rejection.

The Office's Utility Examination Guidelines require:

> Any rejection based on lack of utility should include a detailed explanation why the claimed invention has no specific and substantial credible utility. Whenever possible, the Examiner should provide documentary evidence (e.g., scientific or technical journals, excerpts from treatises or books, or U.S. or foreign patents) to support the factual basis for the prima facie showing of no specific and substantial credible utility. If documentary

> evidence is not available, the Examiner should specifically explain the scientific basis for his or her factual conclusions.

(Guidelines at §B.3.). Appellant submits that the rejection does not specifically explain a scientific basis to doubt the asserted utility. To the contrary, in making the subject rejection, the Office turns the burden, which the Office's own rules specifically places on itself, onto the applicant/appellant, requiring proofs, even though it was admitted in a previous rejection that transforming a cell *in vivo* is enabled when done with a stent or balloon catheter, and it is admitted in the final rejection that transforming a cell *in vitro* is enabled. For instance, the Office essentially asks the applicant/appellant to explain how the nucleic acid entrapped in fibrin gel can be taken up by cells. Appellant respectfully notes that even the most skilled in the art can offer no more than informed speculation on the mechanism of transformation. Such is not a requirement of the patent law. That is, the patent law does not require an applicant to understand the theory of operation for his or her invention. Moreover, there is no requirement that an applicant show every possible way there is to perform his invention.

Further, according to the Guidelines, the Office's showing must contain the following:

(1) An explanation that clearly sets forth the reasoning used in concluding that the asserted specific and substantial utility is not credible;

(2) Support for factual findings relied upon in reaching this conclusion; and

(3) An evaluation of all relevant evidence of record, including utilities taught in the closest prior art.

(Guidelines at §B.3.(b).). In other words, the Office must establish that "it is more likely than not that a person skilled in the art would not consider credible any specific and substantial utility asserted by the applicant for the claimed invention." Guidelines at §B.3.(b).

The subject rejection does not meet even the minimal requirements of the Utility Guidelines.

The Court of Appeals for the federal Circuit has reiterated that:

> [A] specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented *must* be taken as in compliance with the enabling requirement of Section 112 unless there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support.

Brana, at 1565, 34 USPQ2d at 1441 (quoting Marzocchi, at 223, 169 USQ at 369). It is:

> *Only* after the PTO provides *evidence* showing that one of ordinary skill in the art would reasonably *doubt* the asserted utility does the burden shift to the applicant to provide rebuttal evidence sufficient to convince such a person of the invention's asserted utility.

Brana, at 1565, 34 USPQ2d at 1441.

Thus, the Office must accept the appellant's assertion of the usefulness of the invention *unless* it provides evidence showing that one of ordinary skill in the art would reasonably doubt the asserted utility, not mere speculation that an invention might not work.

II. Conclusion

For the reasons set forth herein, it is urged that the rejections of claims 1 and 13-16 should be reversed. Allowance of this application with claims 1 and 13-16 is in order. Such action is earnestly solicited.

Respectfully submitted,

Bristol-Myers Squibb Company
Patent Department
100 Headquarters Park Drive
Skillman, NJ 08558
(908) 904-2372

Date: May 3, 2005

John M. Kilcoyne
Attorney for Appellant
Reg. No. 33,100

APPENDIX

1. A method of transforming a cell comprising, in order, the steps of:

applying a transformation effective amount of a nucleic acid to the cell;

adhering a pliable, adhesive fibrin gel to the cell so as to entrap a transformation effective amount of the nucleic acid in the fibrin gel adhered to the cell; and

transforming the cell with the nucleic acid.

13. The method of claim 1, wherein the nucleic acid is a plasmid.

14. The method of claim 1, wherein the nucleic acid is incorporated in a virus.

15. The method of claim 1, wherein the pliable, adhesive fibrin gel is formed by mixing a fibrin monomer composition with a polymerizing agent preparation effective to convert the fibrin monomer preparation into a fibrin gel, and adhered by contacting the cell with the mixture while the mixture is pliable and adhesive.

16. The method of claim 15, wherein the fibrin monomer composition comprises acid-solubilized fibrin, and the polymerizing agent comprises an amount of base effective to sufficiently neutralize the mixture to allow the fibrin to polymerize.